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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/519,076 | 03/06/00 | SALKOFF | 8512-001305 |

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TOWNSEND AND TOWNSEND AND CREW
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO CA 94111-3834

HM22/1023

| EXAMINER |
|---|
| BASI,N |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | 7 |

DATE MAILED: 10/23/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/519076 | Lawrence Salkoff et al |
| **Examiner** | **Group Art Unit** |
| Nirmal S Bajwa | 1646 |

*—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—*

**Period for Response**

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

**Status**

☐ Responsive to communication(s) filed on 8/2/01.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

**Disposition of Claims**

☒ Claim(s) 1-17, 19, 21-56 is/are pending in the application.

Of the above claim(s) 1-16, 22-44 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 17, 19, 21, 45-56 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

**Application Papers**

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119 (a)-(d)**

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

**Attachment(s)**

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2

☐ Interview Summary, PTO-413

☐ Notice of References Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

**Office Action Summary**

## DETAILED ACTION

1. Amendment /Response to Restriction requirement filed 8/2/01 has been entered.

### *Election/Restriction*

2. Applicant's election with traverse of Group III (Claims 17, 19 and 21), in Paper No. 6 (8/2/01), is acknowledged. The traversal is on the ground(s) that Groups I-IV encompass orthologous and allelic sequences of the same gene or its encoded protein, Groups fall within same class and subclass and the genus of proteins is claimed on the basis of the common structural and functional features and the examining of I-XVI would not place a substantially greater burden on the examiner. Applicants arguments have been fully considered but not found persuasive. Applicant has not disclosed the genes for any of the claimed polynucleotides, only cDNA. The protein and nucleic acid encompassed by the claims, although being potassium channels, are structurally and functionally distinct inventions. There is no disclosure showing that all the channel proteins have the same function as a result of the potassium transport. There is no disclosure of the critical structural features encompassed by the polypeptides and polynucleotides of instant invention that would warrant their them being grouped together. Applicant has not disclosed what structural feature of the polypeptides and polynucleotides is responsible for ion transport and the physiological function. Therefore a search of groups I-XVI would not be co-extensive particularly with regard to the literature search, each sequence of the channel protein requires a separate search. An examination of the materially different, patentably distinct inventions in a single application would constitute a serious undue burden on the examiner.

The requirement is still deemed proper and is therefore made FINAL.

In the Amendment /Response to Restriction requirement filed 8/2/01 Applicant has amended claims 17, 19, 21 and added new claims 45-56. Claims 17, 19, 21 and 45-56 will be examined as they encompass the elected Group III, pertaining to purified polypeptide comprising amino acid sequence of SEQ ID NO:16, being encoded by the nucleic acid of SEQ ID NO:17. Claims 17, 19, 21 and 45-56 contain non elected inventions, encompassing the polypeptides and polypeptides of SEQ ID NOs:1, 2, 3, 4, 18 and 19, see paper number 5 (6/29/01). Applicant must amend the claims to remove reference to non-elected invention. Accordingly, claims 1-16, 18, 22-44 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

**Claim Rejection, 35 U.S.C. 112, second paragraph**

3. Claims 17,19, 21 and 45-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 45, 50 and 55 are indefinite because the method of determining the molecular weight has not been identified. A value for the molecular weight is entirely dependent upon the method by which it is determined and differs with different methods (e.g. denaturing gel, native gel, calculated from amino acid sequence, gel filtration etc.). Recitation of a molecular value without reference to the method by which it was measured is indefinite.

Claims 17 is indefinite because the antibodies can not be generated against SEQ ID NO:s: because the sequences are mere characters on a page. It is suggested that the claim be amended to include language such as, "generated against the polypeptide disclosed in SEQ ID NO:16". Further it is not clear what is "specifically binding to polyclonal antibodies", so as to allow the metes and bounds of the claim be determined. The specification discloses, the phrase "specifically (or selectively) binds to an antibody" when referring to a protein or peptide, "refers to binding reaction that is determinative of the presence of the protein in a heterogenous population of proteins and other biologics". The specification further states, "Thus, under designated immunoassay conditions, the specified antibodies bind to a particular protein and do not bind in a significant amount to other proteins present in the sample", (page 26). Therefore from the definition of "specifically binding", provided in the specification, it is not clear what is the "significant amount" of "other proteins present in the sample" to which the antibody does not bind. Since "specifically binding" dictates which polypeptide are encompassed by the claim the metes and bounds of the claims cannot be determined without a clear definition of said specific binding.

Claims 17, 46 and 52 are indefinite because it is not clear when polypeptide has "unit conductance of approximately 80-120 ps when the monomer is in a functional tetrameric form". The metes and bounds of the group of polypeptides that would meet the limitations of the claim depend upon the precise conditions under which the "unit conductance" is determined. Since the conditions under which the "unit conductance" is determined dictate which polypeptide are encompassed by the

claim the metes and bounds of the claims cannot be determined without the disclosure of said conditions.

Claims 17, 46 and 52 are indefinite because it is not clear what is "approximately intracellular pH of 7.1" and "approximately 80-120 pS". Instant invention is a pH sensitive potassium channel, it sensitivity to pH fluctuations and the conductance measured under specific conditions determines the metes and bounds of the group of polypeptides that would meet the limitations of the claim. The pH and conductance are critical features of the invention and dictate which polypeptide are encompassed by the claim the metes and bounds of the claims cannot be determined without the disclosure of the metes and bounds of "approximately". It is not clear when is the intracellular pH is approximately 7.1 and unit conductance approximately 80-120 pS as compared to when intracellular pH is not approximately 7.1 and unit conductance is not approximately 80-120 pS.

Claims 17, 47 and 52 are indefinite because it is not clear what activity is increased, so as to allow the metes and bounds of the claims to be determined.

Claim 17, 47 and 52 are indefinite because it is not clear what must be combined with the monomer to form the "functional tetrameric form" and what function the tetrameric form has, so as to allow the metes and bounds of the claims to be determined. What else in addition to the monomer is required form the "functional tetrameric form".

Claim 52 is indefinite because the nucleic acid cannot hybridize to "a nucleic acid sequence of SEQ ID NO:" because the sequences are mere characters on a page. It is suggested that the claim be amended to include language such as, "to the nucleic acid disclosed in SEQ ID NO:17".

Claims 19, 48 and 53 are indefinite because it is not clear what is the amino acid of a human or mouse Slo3. Since the name Slo3 is not an art accepted description of the proteins it does not sufficiently describe said proteins. The name human or mouse Slo3 do not provide any structural limitations so as to allow the metes and bounds of the claim to be determined. It is suggested Slo3 be identified by SEQ ID NO:.

Claims 17, 19, 21, 47, 48, 49, 52, 53 and 54 are rejected because they contain to non elected inventions of SEQ ID Nos:1, 2, 3, 4, 18 and 19. Applicant must amend the claims to claim the elected invention.

Claims 46, 51, 55 and 56 are indefinite for depending on an indefinite base claim or intermediate claim and fail to resolve the issues raised above.

***Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph***

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 17, 19 , 21 and 45-56 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

A "specific utility" is a utility that is specific to the subject matter claimed, as opposed to a "general utility" that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A "well established utility" is a utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. A "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention.

Applicant has asserted utilities for the specifically claimed invention of claims 17, 19 , 21 and 45-56.

The claims are directed to isolated polynucleotide comprising a sequence encoding the polypeptide of: a) SEQ ID NOs: 16 or other proteins which have specific functional features associated with the claimed pH sensitive potassium channel.

It appears from the specification that the nucleic acid of SEQ ID NOs: 17 encodes the polypeptide (SEQ ID NO:16) of a pH sensitive potassium channel, the monomer having a unit conductance of approximately 80-120 pS, under specific conditions, when expressed in *Xenopus* oocytes. The polypeptide of SEQ ID NO:16, when expressed in *Xenopus* oocytes, in suggested to

form a functional tetrameric complex, capable of transporting potassium ions, having increased potassium ion transporting activity above an intracellular pH of 7.1, specifically binding to polyclonal antibodies generated against a polypeptide comprising an amino acid sequence of SEQ ID NO:16 (encoded by the DNA of SEQ ID NOS:17). The applicant has mentioned general functional activities which may be applicable to known pH sensitive potassium channel proteins but not disclosed the function associated with the specific proteins encoded by the claimed nucleic acids. The specification discloses potassium channels are found in a wide variety of animal cells and "channels regulating these currents open and allow the escape of potassium under certain conditions". Potassium channels are also disclosed to be "involved in diverse functions such as regulating arteriolar smooth tone" and "tuning of hair cell frequency, and modulation of transmitter release at nerve terminals". The specification further discloses:

a) Potassium channels have evolved to play specialized roles in many excitable tissues,

b) Slo3 (protein of SEQ ID NO:16 encoded by nucleic acid of SEQ ID NO:17), a pH sensitive potassium channel with novel functional properties, is abundantly expressed in speramatocytes. Unlike other members of Slo family, Slo3 channels are not gated by calcium, exhibit markedly lower selectivity for $K^+$ over $Na^+$ than most voltage-gated $K^+$ channels (page 3) .

c) The physiological reactions that sperm undergo to achieve fertilization include changes in both pHi and membrane potential. Slo3 can be used for assaying for compounds that increase or decrease the ion channel activity of this pH sensitive potassium channel, which is involved in sperm physiology. Inhibitors or activators identified may be used therapeutically to treat infertility conditions related to

sperm physiology, or as contraceptives (page 12). Slo3 can be used to study sperm physiology or used to identify homologs, variants or mutations of the channel that may be associated with disease.

Although the claimed polypeptide of instant application encode potassium channels the specific result of changing potassium flux is not known. The specification discloses the Slo3, pH sensitive potassium channels can be used in screening inhibitors and activators, in methods of identifying homologs, in cellular transfection, and gene therapy. In light of the specification the skilled artisan can speculate that the polypeptide (SEQ ID NO:16) encoded by polynucleotide (SEQ ID NO:17) are pH sensitive potassium channel proteins, and nucleic acid that hybridize to the disclosed nucleic acids of SEQ ID NOS:17 or the antibody of claim 17, may belong to the pH sensitive potassium channel proteins. However, apart from the disclosure of the polypeptide of SEQ ID NOS:16 no other disclosure is provided within the instant specification on what the functional features the protein encoded by the claimed polynucleotides, nor are any disease states disclosed that are directly related to its dysfunction. Unlike other members of Slo family, Slo3 channels are not gated by calcium, exhibit markedly lower selectivity for $K^+$ over $Na^+$ than most voltage-gated $K^+$ channels, they must therefore play a specialized role in cell function. There is no disclosure of the specialized role played by the claimed polypeptide in excitable tissues. Showing that the claimed protein can transport ions is not sufficient to show either a specific and substantial asserted utility or a well established utility. Many proteins transport ions, but have very different effects. What is the physiological function that occurs as a result of the ion transport by the claimed polypeptide.

The utilities asserted by Applicant are not specific or substantial. Since no specific function of the polypeptides of instant invention, or polynucleotides that encode them, are known, and the hypothesized function is based entirely on conjecture from homologous polypeptides, the asserted utilities are not specific to instant polypeptide, but rather are based on family attributes. Neither the specification nor the art of record disclose the claimed nucleic acids, useful to identify drugs that affect said proteins and modulate their activity. Similarly, neither the specification nor the art of record disclose any instances where disorders can be effected by interfering with the activity using claimed polynucleotides. Thus the corresponding asserted utilities are essentially methods of using the claimed polynucleotide to identify other nucleic acids that hybridize to said polynucleotide, or to isolate disease states associated with polypeptide disfunction, and as targets for drug discovery. Therefore the asserted utilities are essentially methods of isolating, testing for or for potentially treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating, isolating or testing for compounds that interact with the claimed polynucleotide, or encoded polypeptide, which may be implicated in an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed polynucleotides, further experimentation is necessary to attribute a utility to the claimed polypeptides and polynucleotide. See Brenner v. Manson, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility'

consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Accordingly, the instant specification provides insufficient guidance on "how to use" the claimed polynucleotide of instant invention.

**Claim Rejection, 35 U.S.C. 112, first paragraph**

5. Claims 17, 19 , 21 and 45-56. are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the polypeptides of instant invention, further experimentation is necessary to attribute a utility to the claimed polynucleotides.

Further isolated polypeptides that bind to polyclonal antibodies generated against the polypeptide of SEQ ID NO:16 or are encoded by nucleic acid which hybridizes to the nucleic acid SEQ ID NO:16 may be unrelated to the Slo3 polypeptide, structurally and functionally. The specification does not disclose the special technical feature of the invention that is required for activity and the claims do not disclose the precise conditions (see rejection under 35 USC 112, second paragraph, above) in which the protein will function as a potassium channel commensurate in scope with the Slo3 channel disclosed in SEQ ID NO:16. Applicant has not disclosed how to use the

variant channel proteins which may have unit conductance of 80-120 ps, some structural similarity to Slo3 of SEQ ID NO:16, but be functionally different.

Also, the claims containing antibodies do not provide a defined structural limitation (antibodies can bind to unrelated proteins, (see rejection under 35 USC 112, second paragraph, above)) and encompasses a variety of subgenera including full-length proteins, chimeric proteins or fusion proteins and variants. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polypeptides, or those of a polypeptide specifically binding to polyclonal antibodies generated against a polypeptide comprising an amino acid sequence of SEQ ID NO:16.. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. No, specific identifying characteristic or property of the afore mentioned polypeptide is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Due to the large quantity of experimentation necessary to identify and purify active proteins encompassed by claims reciting hybridization and antibody language, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said polypeptides, the unpredictability of the effects of mutation on the structure and function of proteins (since mutations of SEQ ID NO:16, are also encompassed by the claim), and the breadth of

the claim which fail to recite precise functional limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention.

7. Claims 17, 19 , 21 and 45-56. are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses the nucleic acid sequence, SEQ ID NO:17, which encode the polypeptide (SEQ ID NO:16) that meets the written description and enablement provision of 35 U.S.C. 112, first paragraph. However, the claims are directed to, or encompass polypeptides that are encoded by nucleic acid that hybridizes to the polynucleotide of SEQ ID NO:17 or polypeptide which bind specifically to the antibody generated against SEQ ID NO:16. None of these polypeptides meets the written description provision of 35 U.S.C. 112, first paragraph. As disclosed in the rejection under 35 USC 112, second paragraph, unit conductance, increased activity and specifically binding to polyclonal antibodies have not been clearly defined, and the conditions to achieve the unit conductance and increased activity that would be possessed by the Slo3 protein of SEQ ID NO:16 are not defined in the claims. Therefore the antibody can bind polypeptides unrelated to SEQ ID NO:16, and said polypeptides can have unit conductance and undefined "increased activity", to that disclosed in the claims, but be unrelated functionally to Slo3. Similarly the polypeptide encoded by nucleic acid that hybridizes to the polynucleotide of SEQ ID NO:17 can have

unit conductance and undefined "increased activity", to that disclosed in the claims, but be unrelated functionally to Slo3.

The claims, as written, encompass polypeptides which vary substantially in length and also in amino acid composition. The instant disclosure of a polynucleotide of SEQ ID NO:17 encoding the polypeptide of SEQ ID NO:16 does not adequately describe the scope of the use of the claimed genus of polypeptides, which encompasses a substantial variety of subgenera including full-length proteins, fragment region bearing polypeptides, epitope region bearing polypeptides, chimeric proteins, fusion proteins, and variants. A description of a genus of polypeptides may be achieved by means of a recitation of a representative number of polypeptides, defined by amino acid sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polypeptides. **There is no description of the conserved regions which are critical to the structure and function of the genus claimed.** For example, what fragments of the polypeptide of SEQ ID NO:16 contain a definitive structural feature required for protein function? What is the "increased activity" stated in claims, what are the conditions required for unit conductance of 80-120 ps, what is functional tetrameric form, what else comprises the tetramer. The specification proposes to discover other members of the genus by using screening assays and techniques involving probes, primers, hybridization. There is no description, however,

of the sites at which variability may be tolerated and there is no information regarding the relation of specific structure to specific function. Structural features that could specifically distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed. No identifying characteristic or property of the instant polypeptides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific polypeptide and nucleotide sequences and the inability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe, enable and use the genus

*Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid or polypeptide is itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

There is insufficient to support the generic claims for reasons given above.

**Advisory Information**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
October 20, 21, 2001

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600